

## Technical report

# A primary care evaluation of three near patient coagulometers

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### Abstract

**Aim**—To compare the reliability and relative costs of three international normalised ratio (INR) near patient tests.

**Materials**—Protime (ITC Technidyne), Coaguchek (Boehringer Mannheim), and TAS (Diagnostic Testing).

**Methods**—All patients attending one inner city general practice anticoagulation clinic were asked to participate, with two samples provided by patients not taking warfarin. A 5 ml sample of venous whole blood was taken from each patient and a drop immediately added to the prepared Coaguchek test strip followed by the Protime cuvette. The remainder was added to a citrated bottle. A drop of citrated blood was then placed on the TAS test card and the remainder sent to the reference laboratory for analysis. Parallel INR estimation was performed on the different near patient tests at each weekly anticoagulation clinic from July to December 1997.

**Results**—19 patients receiving long term warfarin treatment provided 62 INR results. INR results ranged from 0.8–8.2 overall and 1.0–5.7 based on the laboratory method. Taking the laboratory method as the gold standard, 12/62 results were < 2.0 and 2/62 were > 4.5. There were no statistical or clinically significant differences between results from the three systems, although all near patient tests showed slightly higher mean readings than the laboratory, and 19–24% of tests would have resulted in different management decisions based on the machine used in comparison with the laboratory INR value. The cost of the near patient test systems varied substantially.

**Conclusions**—All three near patient test systems are safe and efficient for producing acceptable and reproducible INR results within the therapeutic range in a primary care setting. All the systems were, however, subject to operator dependent variables at the time of blood letting. Adequate training in capillary blood sampling, specific use of the machines, and quality assurance procedures is therefore essential.

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Oral anticoagulation management is developing outside the traditional hospital setting, primarily because of increased indications for anticoagulation treatment including non-rheumatic atrial fibrillation.<sup>1,2</sup> One Birmingham study has shown that nurse led primary care anticoagulation clinics can be developed, with international normalised ratio (INR) measurement determined by near patient testing.<sup>1</sup> This model would be suitable for most primary health care settings in many countries.

While several near patient test systems are available for INR estimation, it is important that the INR can be measured reliably within primary care settings, given the difficulties already established with laboratory standardisation.<sup>3–5</sup>

Three near patient test devices—Protime (ITC Technidyne), Coaguchek (Boehringer Mannheim) and TAS (Diagnostic Testing)—have been shown to be robust and reliable in comparison with standard laboratory INR techniques.<sup>6–8</sup> In this study we compared these three near patient test coagulometers for INR estimation in a primary care setting. We report the results obtained on venous blood samples using the three systems, in addition to a sample sent to the local reference laboratory. The local reference laboratory (Queen Elizabeth Hospital, Birmingham) used an ACL 2000 system with IL reagent, and was taken as the gold standard for the study. The laboratory performs consistently within consensus in the national external quality assessment scheme (NEQAS) anticoagulation assessment. Although a true gold standard does not exist, the laboratory was used as the criterion to judge the validity of the three near patient test systems in this study in terms of realistic performance expectations, attention to preanalytical sample handling, and personnel requirements. The objectives of the study were to evaluate the reliability in terms of INR measurement of three near patient testing machines; to evaluate any technical difficulties encountered; to compare the costs of the near patient test machines; and to compare the quality assurance procedures for each machine.

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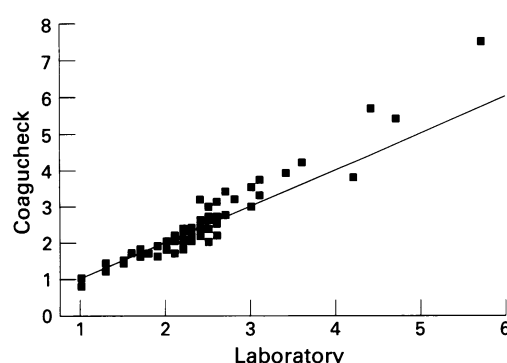


Figure 1 Scatter plot of Coaguchek versus laboratory INR results.

### Methods

The study was based in one primary care anticoagulation clinic in an inner city general practice. The clinic was managed by a practice nurse with previous near patient test experience. Patients attending the clinic who had been receiving warfarin for at least six months were eligible for the study. Housebound patients were excluded. Patients were asked to participate and to consent to the venous samples required for the three near patient tests. They were informed that warfarin management would be based on the same near patient tests consistently (Coaguchek). The evaluation was performed following the criteria determined by the near patient testing working party of the British Society of Haematology, including samples across the whole therapeutic INR range, with samples from patients not receiving warfarin and samples above the upper limit of the therapeutic range.<sup>9</sup>

### PROCEDURE

- The three near patient test systems were prepared and test cards, reagent strips, and cuvettes held at room temperature for 10 minutes before use.
- Internal quality control (QC) was performed on the Coaguchek (CK) and TAS machines with control material supplied by the manufacturers, and the Protime was switched on to "self check and calibrate."

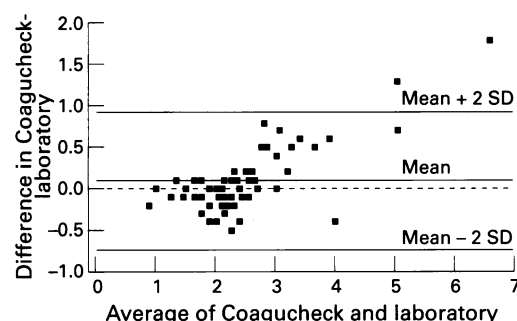


Figure 2 Bland-Altman plot of Coaguchek versus laboratory data.

Table 1 Differences in the international normalised ratio between the four methods used (n=62)

	Coaguchek	Protime	TAS
Laboratory	-0.10 (0.05) / 0.960	-0.28 (0.06) / 0.921	-0.10 (0.06) / 0.912
Coaguchek		-0.19 (0.05) / 0.951	0.00 (0.05) / 0.937
Protime			0.19 (0.06) / 0.906

Values are mean (SE) difference / correlation coefficient.

- Five millilitres of venous whole blood were taken, and a drop immediately added to the Coaguchek test strip followed by the Protime cuvette. The remainder was added to a citrated bottle and mixed well. A drop of citrated blood was then added to the TAS test card and the remainder sent to the reference laboratory for analysis.

- All INR results were recorded centrally.

Parallel INR estimation was performed on the different near patient tests at each weekly anticoagulation clinic from July to December 1997. Paired *t* tests, regression analysis, and Bland-Altman plots were undertaken to investigate the agreement between the results obtained between the three near patient test systems and the laboratory, although not all methods are reported. The results were also analysed to determine the number of times dose adjustment would have been made depending on whether near patient test values or the laboratory INR value were used.

### Results

Nineteen patients (including two not taking warfarin) provided 62 samples for analysis. INR results ranged from 0.8 to 8.2 overall, and 1.0 to 5.7 based on the laboratory method. Taking the laboratory method as the gold standard, 12 of the 62 results were < 2.0 and six were > 4.5. The largest proportion of patients were receiving warfarin treatment for atrial fibrillation (47%), followed by mitral valve replacement (26%). Approximately 50% of patients were under 65 years of age.

### INR COMPARISONS

There were no statistical or clinically significant differences in terms of correlation coefficients (fig 1) or Bland-Altman plots (fig 2) between results from the three systems, although all near patient tests showed slightly higher mean readings than the laboratory (table 1). In terms of clinical decisions, 12 of 62 dosing decisions (19%) would have been altered when comparing Coaguchek and TAS with the laboratory, and 15 of 62 (24%) when comparing Protime with the laboratory.

### TECHNICAL DIFFICULTIES

Table 2 describes the three near patient test systems used in the evaluation, in terms of how the specimen is collected and measured, the quantity and type of blood used for the collection, the reagent properties, and the quality control and calibration methods. No mechanical problems were encountered with any of the machines, and robustness had previously been evaluated for all of them.<sup>6-8</sup> All three near patient test systems were simple and user friendly. The Protime system takes longer to produce a result (up to six minutes), as this includes quality control procedures integral to the test, whereas the other machines require a QC procedure before patient testing begins. The Coaguchek and TAS require only a small quantity of blood and therefore with capillary sampling there is less risk of an inadequate sample. The amount of blood required by the Protime is quite substantial (65 µl) and

Table 2 Description of near patient test (NPT) systems

Feature	System		
	Coaguchek	TAS	Protime
Specimen collection:	Test strip/iron oxide particles/thromboplastin	Test card/magnetic strip/iron oxide particles/thromboplastin	Test cuvette/Tenderlett device/cuvette containing thromboplastin
Quantity of blood:	Approx 45 µl	30–35 µl	Approx 65 µl
Detection principle:	Iron oxide particles/ photoreflexion	Iron oxide particles/ photoreflexion	Photopic detection of decreased blood flow
Type of blood:	Whole blood, venous or capillary	Citrated whole venous blood or plasma	Whole blood, venous or capillary
Thromboplastin:	Rabbit brain	Human placenta	Recombinant
Memory store:	30 test results	1000 test results	39 test results
IQC:	Supplied by manufacturer	Integral to machine and supplied by manufacturer	Integral to test cuvette
EQC:	NEQAS scheme	NEQAS scheme	Not considered necessary by manufacturer
Calibration:	Lot specific code chip new test strips	Integral to magnetic strip on test card	Instrument and cuvettes precalibrated

EQC, external quality control; IQC, internal quality control; NEQAS, National external quality assessment scheme.

therefore with poor fingerstick technique there is a risk of an inadequate capillary sample. Otherwise, each system has built in error coded for operator mistakes. Both the Coaguchek and Protime can use either venous or capillary samples. TAS at the time of the study required citrated whole blood or plasma; however, the manufacturers have recently produced test cards for non-citrated samples.

#### COSTS

The cost of the different systems varied substantially (table 3). The test reagents of two machines were comparable, but the Protime system was more expensive. However, the Protime reagent cuvette has a built in lancet device which precludes additional costs for finger pricking equipment.

#### QUALITY ASSURANCE PROCEDURES

For Coaguchek, calibration and internal quality control systems are quick and simple to use at the start of each clinic. External quality control is available through NEQAS, although this only offers comparison with other Coaguchek users. For Protime, calibration and two levels of internal quality control are integral to each test performed. External quality control is unnecessary according to the manufacturers. NEQAS, however, suggest sending a comparison venous sample to the laboratory every 10 tests. For TAS, the system performs self diagnostic tests to verify the hardware integrity, and calibration is performed on each test card. Quality control is performed with each test by checking test card validation, date and time verification, sufficient sample verification, and sample type verification. A control plasma test is also performed before each clinic. External quality assurance for TAS is available through NEQAS.

#### OTHER FACILITIES INCORPORATED

All three systems have menu options for date and time and memory capability for at least 30

previous results. They also have the capability to link to both a printer and computerised decision support software. Protime offers a graphical display of patient results within therapeutic range for patients performing home monitoring, which gives a clearer idea of their INR control. TAS offers a menu option for operator identity so that aberrant results can be traced to the operator. It has memory capability for up to 1000 previous results. All three systems offer at least a 12 month warranty and a service contract, with a promise of a replacement machine. Both Coaguchek and Protime are small and lightweight with the facility to be battery operated for increased portability. TAS, in contrast, is heavier and therefore less appropriate for domiciliary use.

## Discussion

### INR COMPARABILITY

Three systems previously validated in laboratory conditions were assessed for use in a non-laboratory setting. The INR results showed no significant disagreement between the systems. Agreement was shown for all therapeutic ranges although, as shown in other studies,<sup>10 11</sup> as absolute INR increases results become more diverse, with near patient test results considerably higher. This was shown consistently in all three systems. Given that management is clinically based under these circumstances, this was not a clinically important finding. Different dosing decisions would have been made on around 20% of occasions. This compares favourably with interlaboratory comparisons, where up to 50% of results would suggest different dose decisions.<sup>12</sup>

All three near patient test systems are therefore safe and efficient for producing acceptable and reproducible INR results within the therapeutic range in a primary care setting. All three systems, however, were subject to operator dependent variables at the time of blood letting. Adequate training in both capillary blood sampling, specific use of the machines, and quality assurance procedures is therefore essential.

### CONCLUSIONS

The three instruments used in this study showed good correlation within the therapeutic ranges, were easy to operate, and required little sample preparation or instrument maintenance. They are all, therefore, appropriate for

Table 3 Comparative costs of near patient test (NPT) systems in practice

	System		
	Coaguchek	Protime	TAS
Cost of NPT system	£730	£900	£2000
Cost of each test	£2.50	£3.50	£2.50
Test available	PT and INR	PT and INR	PT, INR, and APTT

APTT, activated partial thromboplastin time; INR, international normalised ratio; PT, prothrombin time.

primary care use as long as the correct procedures are followed. The near patient testing site, in liaison with the local reference laboratory, should take responsibility for assessing the accuracy and precision of the machines and it is essential to have standard operating procedures developed to ensure optimum care.

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